Answer 1:

**Bibliographic Information**

**Luteinizing hormone-releasing hormone agonist limits DU-145 prostate cancer growth by attenuating epidermal growth factor receptor signaling.** Wells, Alan; Souto, Jose Carlos S.; Solava, James; Kassis, Jareer; Bailey, Karlyn J.; Turner, Timothy. Department of Pathology, Pittsburgh VAMC and University of Pittsburgh, Pittsburgh, PA, USA. Clinical Cancer Research (2002), 8(4), 1251-1257. Publisher: American Association for Cancer Research, CODEN: CCREF4 ISSN: 1078-0432. Journal written in English. CAN 137:73784 AN 2002:359666 CAPLUS 

**Abstract**

Because autocrine EGF receptor (EGFR) stimulation exists in most, if not all, prostate carcinomas and is required for cell proliferation, the authors asked whether LHRH signaling cross-attenuated EGFR to limit tumor growth in the human prostate carcinoma cell line DU-145. One possible mechanism was suggested by LHRH receptors triggering phospholipase-C (PLC) to activate protein kinase C (PKC) because PKC activation limits EGFR tyrosine kinase activity by phosphorylating EGFR at threonine 654. The role of this cross-attenuation mechanism was studied by mutating the threonine 654 amino acid to an alanine (A654) to abrogate this inhibition. DU-145 cells stably expressing wild-type and A654 EGFR were grown as xenografts in the s.c. space of athymic mice. DU-145 cells, overexpressing wild-type EGFR, formed tumors in athymic mice that were inhibitable by goserelin acetate (Zoladex). Tumors expressing the A654 EGFR were resistant to this growth inhibition. These results paralleled in vitro studies in which goserelin acetate blocked proliferation of the WT DU-145 but not A654 DU-145 cells. These data support the model of LHRH agonists preventing EGFR-mediated tumor growth through a PKC pathway. This suggests new targets of modulatory intervention to limit the growth of androgen-independent prostate carcinomas.